

## WHAT IS CLAIMED IS:

1. A protein having a formula selected from the group consisting of:  $R_1-R_2$ ,  $R_2-R_1$ ,  $R_1-L-R_2$ , and  $R_2-L-R_1$ , wherein  $R_1$  is a Fc protein, or variant or fragment thereof,  $R_2$  is an OPG protein, or variant or fragment thereof, and L is a linker.

2. The protein of Claim 1 having the formula  $R_2-L-R_1$ .

3. The protein according to claim 1, wherein the Fc protein is selected from the group consisting of:

(a) the Fc amino acid sequences as set forth in Figure 1; (561981)

(b) the amino acid sequence of subpart (a) having a different amino acid substituted or deleted in one or more of the following positions (using the numbering according to Figure 1):

- (i) one or more cysteine residues;
- (ii) one or more tyrosine residues;
- (iii) cysteine at position 5 deleted or substituted with an alanine;
- (iv) leucine at position 20 deleted or substituted with glutamine;
- (v) glutamic acid at position 103 deleted or substituted with an alanine;
- (vi) lysine at position 105 deleted or substituted with an alanine;
- (vii) lysine at position 107 deleted or substituted with an alanine;
- (viii) deletion or substitution of one or more of the amino acids at positions 1, 2, 3, 4, and 5;

(ix) one or more residues substituted or deleted to ablate the Fc receptor binding site;

(x) one or more residues substituted or deleted to ablate the complement (C1q) binding site; and

(xi) a combination of subparts i-x;

(c) the amino acid sequence of subparts (a) or (b) having a methionyl residue at the N-terminus;

(d) the Fc protein, or variant, fragment or derivative thereof, of any of subparts (a) through (c) comprised of a chemical moiety connected to the protein moiety;

(e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;

(f) a derivative of subpart (e) wherein said water soluble polymer moiety is polyethylene glycol; and

(g) a derivative of subpart (e) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.

4. The protein according to claim 1, wherein the OPG protein or variant, fragment or derivative thereof, is selected from the group consisting of:

(a) the amino acid sequence 22-X wherein X is any residue from position 185 to 401 inclusive as shown in Figure 2 (SEQ ID NO: 2);

(b) the amino acid sequence 22-X wherein X is any residue from position 185 to 293 inclusive as shown in Figure 2 (SEQ ID NO: 2);

(c) the amino acid sequence of subparts (a) and (b) having a methionyl residue at the N-terminus.

(c) the OPG protein, or variant, fragment or derivative thereof, of any of subparts (a), (b) and (c) comprised of a chemical moiety connected to the protein moiety;

5 (d) a derivative of subpart (c) wherein said chemical moiety is a water soluble polymer moiety;

(e) a derivative of subpart (d) wherein said water soluble polymer moiety is polyethylene glycol;

10 (f) A derivative of subpart (d) wherein said water soluble polymer moiety is a polyamino acid moiety; and

(g) a derivative of subpart (d) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.

20 5. The protein of claim 1 wherein the linker is one or more amino acids selected from the group consisting of glycine, asparagine, serine, threonine and alanine.

6. The protein of claim 1 wherein the linker is selected from the group consisting of:

- 25 (a) ala-ala-ala; (SEQ ID NO:51)  
 (b) ala-ala-ala-ala; (SEQ ID NO:52)  
 (c) ala-ala-ala-ala-ala; (SEQ ID NO:53)  
 (d) gly-gly; (SEQ ID NO:54)  
 (e) gly-gly-gly;  
 (f) gly-gly-gly-gly-gly; (SEQ ID NO:55)  
 30 (g) gly-gly-gly-gly-gly-gly-gly; (SEQ ID NO:56)  
 (h) gly-pro-gly;  
 (i) gly-gly-pro-gly-gly; (SEQ ID NO:57)  
 (j) val;  
 35 (k) ser-gly-gly-gly-gly-gly-gly-gly-gly-gly; (SEQ ID NO:58)

gly; (SEQ ID NO:58)

B  
B  
B  
B  
B

B (1) gly-gly-ser-gly-ser-ala-gly-ser-  
gly-ser-gly-gly-gly-ser-gly-ser-gly-gly- (SEQ ID NO: 57)

(m) a chemical moiety; and

(n) any combination of subparts (a)  
5 through (m).

7. A fusion protein comprising the amino  
acid sequence selected from the group consisting of the  
amino acid sequences set forth in Figures 5, 6, 7 or 8  
10 (SEQ ID NOS: 5, 6, 7, 8, respectively).

8. A nucleic acid sequence encoding for a  
protein having the formula selected from the group  
consisting of:  $R_1-R_2$ ,  $R_2-R_1$ ,  $R_1-L-R_2$ , and  $R_2-L-R_1$  wherein  
15  $R_1$  is a Fc protein, or variant or fragment thereof,  $R_2$   
is an OPG protein, or variant or fragment thereof, and  
L is a linker.

9. The nucleic acid sequence of Claim 8  
20 encoding for a protein comprising an Fc protein,  
variant, fragment or derivative portion selected from  
the group consisting of:

(a) the Fc amino acid sequence as set forth  
in Figure 1 (SEQ ID NO: 1);

25 (b) the amino acid sequence of subpart (a)  
having a different amino acid substituted or  
deleted in one or more of the following positions  
(using the numbering according to Figure 1):

- 30 (i) one or more cysteine residues;  
(ii) one or more tyrosine residues;  
(iii) cysteine at position 5 deleted or  
substituted with an alanine;  
(iv) leucine at position 20 deleted or  
substituted with glutamine;  
35 (v) glutamic acid at position 103  
deleted or substituted with an alanine;

(vi) lysine at position 105 deleted or substituted with an alanine;

(vii) lysine at position 107 deleted or substituted with an alanine;

5 (viii) deletion or substitution of one or more of the amino acids at positions 1, 2, 3, 4, and 5;

(ix) one or more residues substituted or deleted to ablate the Fc receptor binding site;

10 (x) one or more residues substituted or deleted to ablate the complement (C1q) binding site; and

(xi) a combination of subparts i-x;

15 (c) the amino acid sequence of subparts (a) or (b) having a methionyl residue at the N-terminus;

20 (d) the Fc protein, or variant, fragment or derivative thereof, of any of subparts (a) through (c) comprised of a chemical moiety connected to the protein moiety;

(e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;

25 (f) a derivative of subpart (e) wherein said water soluble polymer moiety is polyethylene glycol; and

(g) a derivative of subpart (e) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.

30 10. The nucleic acid sequence according to claim 8 encoding for a protein comprising an OPG protein, variant, fragment or derivative portion selected from the group consisting of:

35 (a) the amino acid sequence 22-X wherein X is any residue from position 185 to 401 inclusive as shown in Figure 2 (SEQ ID NO: 2);

(b) the amino acid sequence 22-X wherein X is any residue from position 185 to 293 inclusive as shown in Figure 2 (SEQ ID NO: 2);

(c) the amino acid sequence of subparts (a) and (b) having a methionyl residue at the N-terminus;

(d) the OPG protein, or variant, fragment or derivative thereof, of any of subparts (a), (b) and (c) comprised of a chemical moiety connected to the protein moiety;

(e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;

(f) a derivative of subpart (e) wherein said water soluble polymer moiety is polyethylene glycol;

(g) A derivative of subpart (e) wherein said water soluble polymer moiety is a polyamino acid moiety; and

(h) a derivative of subpart (e) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.

11. The nucleic acid sequence of claim 8 encoding for a protein comprising a linker of one or more amino acids selected from the group consisting of glycine, asparagine, serine, threonine and alanine.

12. The nucleic acid sequence of claim 8 encoding for a protein with a linker selected from the group consisting of:

- (a) ala-ala-ala;
- (b) ala-ala-ala-ala;
- (c) ala-ala-ala-ala-ala;
- (d) gly-gly;
- (e) gly-gly-gly;
- (f) gly-gly-gly-gly-gly;

- (g) gly-gly-gly-gly-gly-gly-gly;  
(h) gly-pro-gly;  
(i) gly-gly-pro-gly-gly;  
(j) val;  
5 (k) ser-gly-gly-gly-gly-gly-gly-gly-gly;  
gly;  
(l) gly-gly-ser-gly-ser-gly-ala-gly-ser-gly-ser-gly-gly-gly-ser-gly-ser-gly-gly;  
(m) a chemical moiety; and  
10 (n) any combination of subparts (a) through (m).

13. A nucleic acid sequence encoding a fusion protein comprising the amino acid sequence  
15 selecting from the group consisting of: the amino acid sequences as set forth in Figures 5, 6, 7 or 8 (SEQ ID NOS: 5, 6, 7, 8, respectively).

14. A vector comprising a nucleic acid  
20 sequence according to any of Claims 8 to 13 inclusive.

15. A prokaryotic or eukaryotic host cell containing the vector of claim 14.

25 16. A process for producing a protein of claims 1 or 6 comprising the steps of culturing, under suitable conditions, the host cell of claim 15, and isolating the protein produced.

30 17. The process of claim 16 further comprising the step of purifying the protein produced.

18. A pharmaceutical composition comprising an effective amount of a protein according to claims 1  
35 or 6, in a pharmaceutically acceptable diluent, adjuvant or carrier.

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